

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

T. Crompton

Serial No: 09/724,964

Filed: November 28, 2000

For: Methods and Compositions for
Regulating Lymphocyte Activity

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Art Unit: Not yet assigned

Examiner: Not yet assigned

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail, postage prepaid, in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231 on the date indicated below:

September 10, 2001

Date of Signature
and of Mail Deposit

Karen DiRocco

Assistant Commissioner of Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Siri:

This amendment is being filed in reply to the outstanding Notice to Comply, mailed August 20, 2001, in connection with the above application. Please enter the following amendments:

In the specification:

Please replace the paragraph from lines 23-29 on page 39 with:

In an exemplary embodiment, portions of the 5' flanking region of the human Shh gene are amplified using primers which add restriction sites, to generate the following fragments

5'-gcgcgttcgaaGCGAGGCAGCCAGCGAGGGAGAGAGCGAGCGGGCGAGCCGGAGC-GAGGAAatcgatgcgc (primer 1) (SEO ID No. 23)

Please replace the paragraph from lines 10-29 on page 40 with:

Individual colonies are selected, cut with AsuII and BamHI, and the size of the AsuII/BamHI fragment determined. Colonies in which both the primer 1 and primer 2 sequences are correctly inserted are further amplified, and cut with AsuII and BamHI to produce the gene activation construct

cgaaggcaggccagcgagggagagcgagcggcgagccggagcgaggaaATCGAAGGTTCGAACCTTC
CCCCACCACCATCACTTCAAAAGTCGAAAGAATCTGCTCCCTGCTGTGTTGG
AGGTCGCTGAGTAGTGCGCGAGTAAAATTAAAGCTACAACAAGGCAAGGCTTGACC
GACAATTGCATGAAGAATCTGCTTAGGGTTAGGCCTTGCCTGCGATGTA
CGGCCAGATATAACCGCTTGACATTGATTATTGACTAGTTATTAAATAGTAATCAATT
ACGGGGTCATTAGTCATAGCCCATAATGGAGTTCCCGCTTACATAACTACGGTA
AATGGCCCGCCTGGCTGACCGCCAACGACCCCCCCCATTGACGTCAATAATGAC
GTATGTTCCCATAAGTAACGCCAATAGGGACTTCCATTGACGTCAATGGGTGGACTA
TTTACGGTAAACTGCCACTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCC
CCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCAGTACATGAC
CTTATGGACTTCCTACTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATG
GTGATGCGGTTTGGCAGTACATCAATGGCGTGGATAGCGGTTGACTCACGGGA
TTTCCAAGTCTCCACCCATTGACGTCAATGGAGTTGGCACCAAATCAA
CGGGACTTCCAAAATGTCGTAACAACCTCCGCCATTGACGCAAATGGCGGTAG
GCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCTGGCTAACTAGAGAACCCA
CTGCTTACTGGCTATCGAAATTACGACTCACTATAGGGAGACCCAAGCTTGGT
ACCGAGCTCGGATCgatctggaaagcgcaagagagagcgcacacaccgcgcactegg (SEQ ID No. 25)

Please replace the first paragraph on page 53 with:

In an illustrative embodiment, the *ptc* therapeutic can be an antisense construct for inhibiting the expression of *patched*, e.g., to mimic the inhibition of *patched* by *hedgehog*. Exemplary antisense constructs include:

5'-GTCCTGGCGCCGCCGCCGTCGCC (SEQ ID No. 26)

5'-TTCCGATGACCGGCCTTCGCGGTGA (SEQ ID No. 27)

5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID No. 28)

The replacement paragraphs presented above incorporate changes as indicated by the marked-up versions below.

In an exemplary embodiment, portions of the 5' flanking region of the human Shh gene are amplified using primers which add restriction sites, to generate the following fragments

5'-gcgcgcttcgaagcgAGGCAGCCAGCGAGGGAGAGAGCGAGCGGGCGAGCCGGAGC-GAGGAAatcgatgcgcgc (primer 1) (SEQ ID No. 23)

5'-gcgcgcagatctGGGAAAGCGCAAGAGAGAGCGCACACGCACACACCCGCCGCG-CACTCGggatccgcgcgc (primer 2) (SEQ ID No. 24)

Individual colonies are selected, cut with AsuII and BamHI, and the size of the AsuII/BamHI fragment determined. Colonies in which both the primer 1 and primer 2 sequences are correctly inserted are further amplified, and cut with AsuII and BamHI to produce the gene activation construct

cgaaggcaggcagccagcgaggagagcgagcgaggcgaggaaATCGAAGGTTGAATCCTTC
CCCCACCACCATCACTTCAAAGTCCGAAAGAACATCTGCTCCCTGCTGTGTTGG
AGGTCGCTGAGTAGTGCGCGAGTAAAATTAAAGCTACAACAAGGCAAGGCTTGACC
GACAATTGCATGAAGAACATCTGCTTAGGGTTAGGCCTTGCCTCGCGATGTA
CGGGCCAGATAACCGTTGACATTGATTATTGACTAGTTATTAAATAGTAATCAATT
ACGGGGTCATTAGTCATAGCCCATAATGGAGTTCCCGCTTACATAACTACGGTA
AATGGCCCGCCTGGCTGACCGCCAACGACCCCCGCCATTGACGTCATAATGAC
GTATGTTCCCATACTAACGCCAATAGGGACTTCCATTGACGTCATGGGTGGACTA
TTTACGGTAAACTGCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCC
CCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCAAGTACATGAC
CTTATGGACTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATG
GTGATGCGGTTTGGCAGTACATCAATGGCGTGGATAGCGGTTGACTCACGGGA
TTTCCAAGTCTCCACCCATTGACGTCATGGAGTTGTTGGCACCAAATCAA
CGGGACTTCCAAAATGTCGTAACAACCTCCGCCCCATTGACGCAAATGGCGGTAG
GCGTGTACGGTGGAGGTCTATAAGCAGAGCTCTGGCTAACTAGAGAACCCA
CTGCTTACTGGCTATCGAAATTAAATACGACTCACTATAGGGAGACCCAAGCTTGGT
ACCGAGCTCGGATCgtctggaaagcgcaagagagagcgacacgcacacccgcccgcgcactcgg (SEQ ID No. 25)

In an illustrative embodiment, the *ptc* therapeutic can be an antisense construct for inhibiting the expression of *patched*, e.g., to mimic the inhibition of *patched* by *hedgehog*. Exemplary antisense constructs include:

5'-GTCCTGGCGCCGCCGCCGTGCC (SEQ ID No. 26)

5'-TTCCGATGACCGGCCTTCGCGGTGA (SEQ ID No. 27)

5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID No. 28)

REMARKS

Applicants submit herewith an amended sequence listing including the sequences noted by the Examiner. Pursuant to the Rules, a hard copy of the sequence listing and a computer readable form of the sequence listing (the diskette) are submitted herewith.

I state that this submission, filed in accordance with 37 C.F.R. 1.821(g) does not include new matter. I further state that the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. 1.821(c) and (e), respectively, are the same.

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

Respectfully Submitted,

Date: September 10, 2001

D.S.P. 3

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